



SDI Review Form 1.6

Journal Name:	Annual Research & Review in Biology
Manuscript Number:	2013_ARRB_7229
Title of the Manuscript:	Initial insight to effect of exercise on maximum pressure in the aortic root using 2D fluid-structure interaction model
Type of the Article	Original Research Article

General guideline for Peer Review process:

This journal's peer review policy states that **NO** manuscript should be rejected only on the basis of '**lack of Novelty**', provided the manuscript is scientifically robust and technically sound.

To know the complete guideline for Peer Review process, reviewers are requested to visit this link:

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PART 1: Review Comments

	Reviewer's comment	Author's comment (if agreed with reviewer, correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)
Compulsory REVISION comments	<p>The authors proposed a model to estimate the maximum pressure in the left ventricle (MPLV). MPLV is an important parameter to measure in different LV diseases. The proposed work is good attempt to estimate MPLV, however the full manuscript needs substantial improvement before considering for publication. Major changes are needed. Please put particular attention how you are using material from previous work and manuscript's structure.</p> <ol style="list-style-type: none"> 1) Introduction needs to be improved. Please organize properly the structure and references. A clear justification for FSI needs to be presented. What FSI do that we cannot get from clinical measurements or other analytical, electrical or numerical models. 2) References must be carefully presented, cited and updated. 3) Please rewrite aims paragraph. As presented, it seems that you already published this work on a previous journal (ref 27). 4) Methods section is messy, and needs to be structured. A workflow diagram may help to better understand your model and clarify what are your inputs and outputs or from where they come. Authors must remind that readers may not be familiar with this numerical approach. 5) Justify why a single volunteer was used, and please clearly show where his data are used. Why his Doppler measurements were not used as input in the 	<ol style="list-style-type: none"> 1) The amendment was applied. Please see Study design and methodology of abstract. 2) References related to mechanical-based measurement were applied. Along with this some other methods including electrical-based method was applied. It should be noted that only those of ones were applied that were able to comparison with our results. 3) There is not significant overlap between current manuscript and ref [27], except for the beginning of both of them. The beginning of this study was changed. For clarifying the ref 27 was attached to be checked. 4) The workflow was added as a figure 1. 5) The main thing you need to know is that the aim of study is to propose a mechanical-based method to assess MPLV. Preliminary results from one subject show data that are in



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	<p>numerical model in a patient-specific way?</p> <p>6) Please consider that patients with cardiopathies may present different hemodynamic and structural alterations, you may acknowledge this issue in the limitations.</p> <p>7) Justify the number of elements used in the model, as well as mesh basic characteristics, and better highlight why patient's specific data are not used.</p> <p>8) Results are presented as a collection of regression models. It is not well justified why authors are presenting them, what we learn from them, what is the relationship with the presented model and evaluated patient. Each presented result must contribute to understand how you are exploring your aims. In general presented results are insufficient.</p> <p>9) Please improve plot presentation and spelling. Legend in the figure must clearly explain the figure. Reader should not guess what is in the figure or from where it comes.</p> <p>10) Justify why LV stroke work or load parameters were not estimated?</p> <p>11) Study finding must be clear set and organized. Again, as you are presenting your work we got the impression that you already published this manuscript or parts of it.</p> <p>12) Section 4.2. can be shorter and better highlight the benefits of the proposed model. Authors claim that electrical-based models has not been used to estimate MPLV. However several works has been published in the last years using simple electrical/analytical models, numerical simulations, etc ... Please look for works from Damien Garcia from University of Montreal, Charles A Taylor from University of Stanford, Lyes Kadem from Corcordia University, and Patrick Segers from University of</p>	<p>good agreement with literature values. The method undoubtedly needs to be validated by more examining, involving independent measurements of intraventricular pressure from different subjects. See conclusion of abstract; see lines 214 and 345.</p> <p>6) That was added (line 317)</p> <p>7) That was clarified. (line 123)</p> <p>8) As it can be seen in figure 1 (workflow diagram) any provided equation should be necessary to acquire MPLV. Along with this, such regression models show us how two parameters are changed to each other (e.g. with polynomial function for COT-Hr at equation 8)</p> <p>9) Legends were amended (please see legends highlighted in yellow) Grammatical errors were corrected and highlighted in yellow. Section of abbreviations was also added.</p> <p>10) It goes without saying that there are a lot of papers in the field of stroke work. Concerning the point that comparing and contrasting them with our probable numerical stroke work could be another original</p>
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	<p>Amsterdam, just to mention some recent authors.</p> <p>13) Please make a major review to your proposed manuscript before submission. Put special attention to you literature review and work structure.</p>	<p>research paper, we consider it for future study.</p> <p>11) Please see ref 27 as attached for you. As it easily can be seen there is not any overlap. And references related to that were cited.</p> <p>12) We again reviewed your suggested studies and even others. Generally, their research involved with mathematical method performed by Matlab software, ultrasound techniques and etc. Most of them assessed pressure gradient instead of value of pressure. The main handicap associated with their electrical model is that electrical based model cannot include dimensions provided by mechanical model. Electrical models are certainly useful to estimate cardiac output and stroke volume, but they are able to assess the other hemodynamics parameters. In fact, no reference has been found focusing on measuring MPLV e.g. by lumped parameter method. On the other hand, it is undoubtedly true that heart valves hemodynamics are mechanical-based rather than electrical-based</p>
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		<p>equations. The more our model becomes mechanical-based, the more our results can be accurate. The significant disadvantage of lumped parameters method is that their method is lack of coordinate system, although certainly our mechanical base simulation can predict hemodynamics regarding its location (X, Y, Z). it goes without saying biological system mechanics differs place to place. Furthermore, Our numerical model is capable of handling with different new inputs such as geometric parameters, pressure boundary conditions despite of its simplicity. It can also be used for studying of different aortic diseases like stenosis that we control the leaflet's tip distance respecting to the severity of aortic stenosis. Changing the pressure boundary conditions, due to such diseases, could be one of model developments.</p> <p>13) The structure was again reviewed and modified.</p>
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<u>Minor</u> REVISION comments	<ol style="list-style-type: none">1) Replace reference 14 for a paper. Such as Sutherland FJ et al. Clin Exp Pharmacol Physiol 2013, 30:867-878, or appropriate reference. Please avoid referring vendors tech notes.2) FSI references may be reduced, please refer to a review FSI/numerical simulation paper or keep only must significant (ex. De Hart)3) Avoid unpublished or submitted references. Please only refer to accepted and published works.4) Please refers in a proper manner used software such as Matlab or Comsol.	<ol style="list-style-type: none">1) That was replaced.2) Concerning the point that our non-invasive method are FSI-based discipline, We believed that giving related details would be necessary.3) Ref [28] was accepted recently and amendment was done.4) Comsol reference was added , ref# 36. They were referred properly in the manuscript.
<u>Optional/General</u> comments	A de novo or resubmission is required. Too many errors, inconsistencies and details are present in the actual manuscript.	